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Practitioner Review: Treatment of Obsessive-Compulsive Disorder in Children and Adolescents

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This paper reviews the treatment of obsessive-compulsive disorder (OCD) in children and adolescents. Focusing on clinical features of the disorder and its treatment particular to pediatric onset, diagnosis, assessment, and behavioral, pharmacological, as well as new investigative treatments are covered. Adaptation of cognitive-behavioral therapy for children and adolescents, use of augmenting agents in drug treatment, and subtyping of OCD cases are developments relevant for current practice.

Keywords: Obsessive-compulsive disorder, anxiety, behavior therapy, children, adolescents, immune disorders, neuropsychiatry, pharmacology.

Abbreviations: ADHD: attention-deficit/hyperactivity disorder; CT: cognitive therapy; CY-BOCS: Children's Yale-Brown Obsessive Compulsive Scale; ERP: exposure and response prevention; IV: intravenous; OCD: obsessive-compulsive disorder; PANDAS: pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection; SC: Sydenham's chorea; SRI: serotonin reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor; TD: Tourette's disorder; Y-BOCS: Yale-Brown Obsessive Compulsive Scale.

Introduction

The last two decades have brought a wealth of new information on the diagnosis and treatment of obsessive-compulsive disorder (OCD) in adult patients. Advances in and availability of behavioral treatments make this a first-line strategy. In addition, there are now a number of effective serotonergic agents which are usually preferred over the tricyclic drug clomipramine, and there is evidence for efficacy of intravenous clomipramine and augmenting effects of other drugs in treatment-refractory patients. Much of this work has been extended to pediatric populations. In children, mounting evidence supports the existence of a subgroup of OCD/Tourette's disorder cases with abrupt onset and/or exacerbation related to group A beta-hemolytic streptococcal infection for whom immunosuppressant therapy appears effective. This review covers the current status of diagnosis and treatment of OCD in children, with reference to information from adult studies as needed.

Diagnosis and Assessment

OCD is characterized by recurrent obsessions or compulsions, or both, that cause impairment in terms of time, distress, or interference in functioning. Even though 50% of cases have their onset by age 15 (Karno & Golding, 1991), pediatric OCD is usually recognized only when severe, typically years after onset (Swedo, Rapoport, Leonard, Lenane, & Cheslow, 1989). Children often keep their OCD secret, and parental report alone underestimates its presence or severity (Rapoport et al., in press). These findings underscore the need for sensitive but direct interviewing of the child about obsessive-compulsive symptoms.

As stressed in recent reviews (D. A. Geller et al., 1998; Shafron, 1998), the symptoms and diagnostic criteria for OCD are very similar in children and adults, except for the recent relative de-emphasis on insight in children about the irrationality of their OCD symptoms (American Psychiatric Association, 1994). Concerns involving family catastrophies, hoarding, contamination, and sexual, somatic, and religious preoccupations are the most common obsessions; washing, repeating, checking, ordering, counting, hoarding, and touching are the most common compulsions in pediatric studies (Geller et al., 1998).

A factorial study in adults found four symptom dimensions: obsessions and checking, symmetry and ordering, cleanliness and washing, and hoarding (Leckman et al., 1997). Hoarding may be less common in children than adults; but in adults, there is evidence that hoarders may be a distinct subgroup who are relatively treatment resistant (Black et al., 1998). Obsessional slowness also is rare in children, but, when present, is very difficult to treat.

Diagnostic assessment of the balance between obsessions and compulsions, the identifiable triggers that may set off these symptoms, and ego-dystonicity of the behaviors are important for planning behavioral strategies. Symptom rating scales such as the Yale-Brown Obsessive Compulsive Scale (Y-BOCS; Goodman et al., 1989) or the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS; Scahill et al., 1997), as well as

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the Children's Version of the Leyton Obsessional Inventory (Berg, Whitaker, Davies, Flament, & Rapoport, 1988) are useful in assessing obsessive-compulsive symptoms and tracking severity over time.

Differential Diagnosis

Normal/developmental rituals. It is important to distinguish OCD from mild rituals and obsessions that occur as developmental phenomena in children (Evans et al., 1997; Leonard, Goldberger, Rapoport, Cheslow, & Swedo, 1990; Zohar & Bruno, 1997). These are relatively easy to distinguish as developmental rituals are not a cause of distress and do not interfere with functioning.

Tourette's/tic disorder. This should be distinguished because the presence of tics, even if mild, also may have implications for treatment. OCD that is comorbid with Tourette's disorder (TD) is a relatively common form of pediatric OCD (Leonard et al., 1992). The differentiation of tics from compulsions can be surprisingly difficult. Some OCD patients may experience seemingly "classical" compulsions as sudden and uncontrollable. Conversely, TD patients may experience a sense of "compulsion" with respect to motor tics, even those patients without comorbid OCD (Leckman, Walker, Goodman, Pauls, & Cohen, 1994; Thomsen, 1998). Family history of tics/TD may also have implications for treatment, regardless of the tic status of the proband. (As discussed under drug treatment, low dose neuroleptic augmentation may be useful for these cases.)

Sydenham's chorea. SC (the neurological variant of rheumatic fever which occurs in response to group A beta-hemolytic streptococcal [GABHS] infection) has been the focus of recent research as it is generally accompanied by OCD and is regularly misdiagnosed as Tourette's (Garvey & Swedo, 1997). SC is characterized by more distal abnormalities of movement such as "milk maid's grasp" and clumsy gait (Garvey & Swedo, 1997).

PANDAS. Based on studies of SC, a subgroup of pediatric OCD cases has been identified and given the acronym PANDAS (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection) (Swedo et al., 1998). PANDAS cases have a dramatic onset and/or later exacerbations of OCD and/or tics in response to infection with group A beta-hemolytic streptococci and are diagnosed by their clinical picture. For these children, the history of two or more OCD and/or tic episodes in association with positive throat culture and/or laboratory evidence of group A beta-hemolytic streptococcal infection has practical implications for treatment. While PANDAS are a focus of much current diagnostic and treatment research in the U.S., it is still not clear how large a proportion of pediatric OCD cases fall under this heading; current estimates are from 5–10% (Swedo, unpublished data).

OCD "spectrum" disorders. A broad spectrum of unwanted repetitive behaviors comprise the presenting symptoms in several disorders not considered to be OCD. These include pervasive developmental disorders and some retardation syndromes in which repetitive "compulsive" behaviors may interfere with functioning, body dysmorphic disorder (particularly face picking), and eating disorders in which food and exercise may be overfocused obsessional concerns. This review does not cover the treatment of these conditions; there is ongoing debate about whether their relationship to OCD is deeper than just clinical similarities, or comorbidity with OCD, and to what extent behavioral and/or drug treatments used for OCD are effective for the obsessive-compulsive phenomena in these conditions (Gordon, State, Nelson, Hamburger, & Rapoport, 1993; Hollander, 1997; Thomsen, 1998).

Trichotillomania. Repetitive hair pulling, classified as an impulse control disorder (American Psychiatric Association, 1994), has the strongest status as an OCD "spectrum" disorder. Trichotillomania has both phenomenological, familial, and treatment characteristics which resemble OCD, and, therefore, is covered briefly here. (See also Hanna, 1997; Swedo & Leonard, 1992; Swedo & Rapoport, 1991.) As with OCD, childhood onset and ego-dystonicity are common. Family data link this condition to OCD, as does comorbidity between hairpulling and OCD per se.

Differential diagnosis may involve excluding *Asperger's disorder*, which is manifested by the development of restricted, repetitive patterns of behavior and interests as well as sustained impairment in social interactions. Content of obsessions would differ for the two disorders. Also, in OCD, there would be normal social development, although severe cases might have social maladjustment secondary to contamination concerns or as a function of carrying out time-consuming rituals.

Some cases of *obsessive-compulsive personality disorder* (OCP) may be confused with OCD. In OCP, there is a generalized pattern of controlling behaviors that is absent in OCD. Also, although not always the case for young children, insight and ego-dystonicity are usually present in OCD. For a minimum of cases, both diagnoses may apply.

A number of *neurological disorders* may, rarely, manifest themselves as OCD. Usually these diagnoses are evident (also see comorbid disorders) such as encephalitides, dystonias, and brain injury (King, Leonard, & March, 1998). These conditions are of theoretical interest as they document various ways in which injury to the basal ganglia/frontal lobe circuitry can precipitate OCD. As mentioned above, SC has been demonstrated to have a high comorbidity with OCD (Garvey, Giedd, & Swedo, 1998).

OCD is highly comorbid, with most studies finding up to 70% of children with OCD to have at least one comorbid disorder (Swedo, Rapoport, et al., 1989; for reviews, see D. A. Geller et al., 1998; King et al., 1998; and Shafron, 1998). Most common are other anxiety disorders, attention-deficit/hyperactivity disorder (ADHD), developmental disabilities, conduct and oppositional disorders, substance abuse, depression, and bipolar disorder.

Comorbidities must be considered in treatment planning, as these conditions affect compliance with treatment. Furthermore, drug treatment for these comorbid disorders may adversely affect the OCD symptoms (see discussion of treatments below). For example, stimulant drugs may exacerbate or even precipitate some obsessive-compulsive behaviors (Borcherding, Keysor, Rapoport, Elia, & Amass, 1990).

Treatment Approaches

Treatment begins with family education about the disorder. Parents need guidance about how to handle their child's behaviors (which may be severely disruptive

Table 1
Selected Studies of Cognitive-Behavior Therapy for OCD in Children and Adolescents

Study	*N*	Age range	Methods	Comments
Piacentini et al., 1994	3	9–13	Psychoeducation for child & family Concurrent family sessions to disengage family from the OCD Ten 2-hr sessions weekly	All improved Gains maintained at 1 yr follow-up
March et al., 1994	15	8–18	Initial education re OCD as an illness Anxiety management training + ERP Parent training Diaries	14 also on drug 10/15 had ≥ 50% improvement 3 nonresponders
Scahill et al., 1996	7	10–15	Visits 1–4: Self monitoring, triggering stimuli ranked, hierarchy established Visits 5–13: ERP (child selects provoking stimuli) Child & parent education weekly Families as cotherapists & informants	5/7 on drug All improved (30–90%) 14 sessions, mostly weekly Booster sessions within 6 mths post-Rx
Wever & Rey, 1997	82	7–19	Training therapists Family/child workbook Family as cotherapist Modified to fit patient's cognitive/developmental level Taped exposure for obsessions Ten sessions across 2 wks, then monthly reviews across 6 mths, then 6-mth follow-ups	57 had combined treatment of whom 22 (39%) weaned off drug
Franklin et al., 1998	14	10–17	Non-random assignment 7: weekly Rx over 4 months 7: 18 sessions over 1 month Parental involvement or individualized	8 on concurrent drugs 12/14 had 50% reduction in Y-BOCs Both weekly and daily sessions effective Maintained at 9-mth follow-up

to family life) and how to avoid punitive responses or the alternative "enabling" that happens when families become enmeshed in rituals. Suggested readings for families could include *OCD in children and adolescents. A cognitive-behavioral treatment manual* (March & Mulle, 1998), which is commonly used by practitioners in the U.S. and other countries. (The original version of this manual was entitled *How I ran OCD off my land.*) In many countries, various OCD patient groups provide information and support and the opportunity for children to meet others with OCD. Caregivers exchange information and are advocates for services. This resource has added considerably to care of OCD and should be considered for all cases. For a model support group, see Black and Blum (1992). In the U.S., the Obsessive-Compulsive Foundation (North Branford, CT) provides such information and support. Other resources include the Obsessive Compulsive Network in Canada; the Obsessive Compulsive Disorder Support Service in Australia, and Obsessive Action, a British charity. On the computer websites www.ocdresource.com and mentalhelp.net/ocd/online.htm, one can obtain basic information on diagnosis, treatment, getting help, and resources such as relevant organizations and suggested readings.

In adults, behavioral and drug treatments have been shown effective for OCD (Hollander, 1997), both singly and in combination. There have been some excellent recent reviews on these topics—behavioral treatment (e.g. Marks, 1997); drug treatment (e.g. Pato, Pato, & Gunn, 1998; Pigott & Seay, 1999). Much of this work has now been extended to children. (For reviews, see, for behavioral treatment: e.g. March, 1995; Shafron, 1998; for drug treatment: e.g. DeVane & Sallee, 1996; Emslie, Walkup, Pliszka, & Ernst, 1999.)

The choice of first-line treatment will depend on the symptom pattern and severity, as well as the patient and family's preference. Whatever is tried, it is important to urge flexibility, as a combination of drug and behavioral treatment may be needed (Greist, 1996; March et al., 1998; O'Connor, Todorov, Robillard, Borgeat, & Brault, 1999; Park, Jefferson, & Greist, 1997; Wever & Rey, 1997).

Cognitive-Behavioral Therapy

Behavioral therapy for OCD has long been documented in adults (Marks, Hodgson, & Rachman, 1975). Since an earlier review (Wolff & Rapoport, 1988), there has been extensive work on how to adapt these techniques to pediatric OCD populations. These will be covered here, with Table 1 showing selected recent systematically conducted studies.

Cognitive-behavioral therapy for OCD encompasses three treatment types: (1) exposure and response prevention (ERP), (2) cognitive therapy (CT), and (3) relaxation training. Of the three, ERP is in the forefront for effectiveness in symptom reduction (Baer & Greist, 1997; Shafron, 1998). CT (e.g. changing false beliefs regarding risk and responsibility, challenging the reality of obsessions and the necessity for compulsions: Emmelkamp & Beens, 1991) is generally viewed as ineffective as

a *sole* treatment for OCD, although it may be helpful in individual cases and if it encourages exposure in a broader CBT program (Shafron & Somers, 1998). Relaxation therapy is used mainly to manage affect during exposure (March, 1995) but has no direct benefit.

ERP for OCD was developed in adults, and the methodology is still undergoing regular refinement (see Greist, 1996; March, 1995). It involves (1) daily exposure to cues avoided because of their inducing discomfort and rituals, and (2) maintaining exposure and not ritualizing for at least an hour or until the discomfort slowly subsides. A minimal trial consists of 10 to 20 hours of treatment with both exposure and response prevention (Baer & Greist, 1997), with *in vivo* (as opposed to fantasy) exposure being optimal (Foa, Steketee, & Grayson, 1985). Although gains from ERP persist beyond its discontinuation, booster treatment may help for long-term progress, and additional treatment may be needed for migration of symptoms and for lapses brought on by stress (Greist, 1996).

Because most clinicians are not trained in behavioral treatment and because of its expense, interactive computer-administered self-assessment and self-help programs for behavior therapy (e.g. BT-STEPS; Baer & Greist, 1997) may be useful (also see Clark, Kirby, Daniels, & Marks, 1998, for a pilot study of computer-assisted ERP in adults), as it can be used by anyone who has a touch telephone. No report of computer-assisted ERP with adolescents has yet appeared, but for some, this could be a promising approach.

ERP has been adapted for children (see Greist, 1996; King et al., 1998; March & Mulle, 1998; Marks, 1997; March, 1995; and Shafron, 1998). Ability to understand the treatment and tolerate the intensity of affect are important considerations (Shafron, 1998). For example, many fear that if they do not engage in compulsive behavior, their anxiety levels will be so high they will "go crazy". Some partially believe in their obsessive concerns about adverse consequences. CT may help manage these feelings. Programs that let the child influence the gradient for exposure to anxiety-provoking stimuli and that help the child externalize the OCD and feel empowered also decrease anxiety (e.g. see March & Mulle, 1998). March and Mulle advise emphasizing to the child that it is the OCD, and not the child, that is the problem. For young children, the OCD may even be given a nasty nickname, and the "good guys" (child, parents, and therapist) work on getting rid of the "bad guys" (the OCD). This type of alliance helps engage the child in treatment.

The family's involvement in the program helps define "ill" interaction patterns versus normal family demands (see Francis & Pinto, 1993) and, of course, is essential for psychological support. Family involvement in CBT itself is also suggested, as the combination of individual sessions plus focused family work, with parents as "co-therapists", generally works best (March, Mulle, & Herbel, 1994).

Comorbidies such as oppositional behavior will call for additional and better-known techniques such as applying a *systematic reinforcement plan*. Owens and Piacentini (1998) describe a boy with disruptive behavior disorder and OCD who had been unsuccessfully treated in two previous medication trials. The boy then was given ERP and a contingency management program for his disruptive behavior so that he could participate in the ERP. There was marked improvement post-treatment and at 2- and 6-month follow-up. Positive reinforcement, such as prizes for completing exposure tasks and reward ceremonies for mastering steps in treatment, also are valuable for most children, whereas punishment increases resistance to treatment (March, 1995).

CBT must be tailored to specific symptoms. For example, ERP is not generally appropriate for scrupulosity and moral guilt or pathological doubt, where CT may be helpful. Contamination fears, symmetry rituals, counting/repeating, hoarding, and aggressive urges are more amenable to ERP. Obsessional slowness appears not to respond well to either behavioral or medication treatment (Wolff & Rapoport, 1988); techniques such as *modeling* (implicitly or explicitly demonstrating adaptive behaviors) and *shaping* (positively reinforcing successive approximations to a target behavior) may be considered (Ratnasuriya, Marks, Forshaw, & Hymas, 1991). Obviously, children who acknowledge the senselessness of their obsessions and rituals are more likely to have better outcomes, as they are more likely to be treatment compliant.

In adults, *patients with pure obsessions* generally have been considered resistant to treatment, with *thought stopping* the "treatment of choice" despite lack of compelling evidence for effectiveness (Freeston et al., 1997). However, a comprehensive CBT program for adult cases with obsessive thoughts and no overt rituals has shown effectiveness (in comparison to waiting list controls) (Freeston et al., 1997). *Massed practice*, using the principle of "semantic satiation" (March, 1995; Marks, 1987), is another suggested technique for pure obsessionals. The individual repeatedly writes out the obsession or says it aloud, or the obsession is recorded on a continuous loop audiotape which is played back repeatedly. The use of loop cassette tapes helps overcome some difficulties patients experience when asked to elicit obsessional thoughts on demand; the tapes provide the necessary control over exposure (Salkovskis & Westbrook, 1989).

Cognitive therapy strategies helping the adolescent patient obtain benign interpretations of intrusive thoughts also may be useful. Shafron and Somers (1998) describe two 14-year-olds who felt that their thoughts were weird and dangerous and that they were going crazy. Therapy included engaging in a simple experiment—trying *not* to think of a white bear. The patients saw that they could be experiencing intrusive thoughts as part of their effort to suppress them, thus universalizing their experience. Each patient gained the perspective that their reactions to their thoughts contributed to the problem. Such *cognitive restructurings* are recommended for patients resistant to ERP.

In general, *trichotillomania* is more difficult to treat than OCD, but behavior therapy is often attempted (e.g. Rapp, Miltenberger, Long, Elliott, & Lumley, 1998; Vitulano, King, Scahill, & Cohen, 1992). Case reports suggest efficacy, but no systematic studies of behavior therapy for trichotillomania could be found. CBT treatment lengths may need to be extended to achieve greater initial symptom reduction, and more focus on relapse prevention may be needed (Lerner, Franklin, Meadows, Hembree, & Foa, 1998).

For children and adolescents, a treatment manual has been developed to facilitate patient and parental compliance, exportability to lay readers and therapists not specifically trained in these techniques, and empirical evaluation of CBT. In an open trial of this program (March et al., 1994), significant benefit was found post-

Table 2
Pharmacologic Treatment for Obsessive-Compulsive Disorder

Drug	Adult dosage	Child/adolescent dosage from controlled study (or best available information)	Duration
First line agents			
Clomipramine	Up to 250 mg/d	Up to 150–200 mg/d[a] (3 mg/kg upper limit)	> 10 wk
Fluoxetine	Up to 100 mg/d	20 mg/d[b]	> 10 wk
Fluvoxamine	Up to 300 mg/d	Up to 200 mg/d[c]	> 10 wk
Sertraline	Up to 200 mg/d	Up to 200 mg/d[d]	> 10 wk
Paroxetine	Up to 60 mg/d	Not known[e]	> 10 wk
Augmenting agents			
Clonazepam	Up to 5 mg/d	Not known	> 4 wk
Haloperidol	Up to 3 mg/d	[Up to 2 mg/d][f]	> 3 wk
Risperidone	[0.5–2.0 mg/d]	[1.5–2.5 mg/d][g]	?

[a] DeVeaugh-Geiss et al., 1992.
[b] Riddle et al., 1992.
[c] Riddle et al., 1996.
[d] March et al., 1998.
[e] Study in progress.
[f] Based on first author's personal experience.
[g] Lombroso et al., 1995.

treatment and at follow-up, and booster treatment allowed medicine discontinuation in a number of the patients. Study of this protocol-driven treatment package is ongoing (see March & Mulle, 1998) and involves the most comprehensive systematic study of its type.

Although none of the behavioral studies described above is truly systematic and controlled, they provided compelling evidence to justify a comprehensive study of CBT's effectiveness in pediatric OCD populations. An ongoing random-assignment collaborative treatment trial being carried out by Drs Edna B. Foa (University of Pennsylvania, PA, U.S.A.) and John S. March (Duke University, NC, U.S.A.), comparing CBT, drug therapy, their combination, and placebo, is now in its third year. Importantly, there will be a sizeable group without concurrent drug treatment, and outcome ratings are "blind" to treatment condition. These data will be important for guiding future treatment in children with OCD.

School. School performance may be impaired by OCD, but school problems may also predate it (D. A. Geller et al., 1998). Certain perfectionist and repeating rituals may severely disrupt performance. For example, the compulsion to reread sentences or entire paragraphs may stop the child from completing assignments. In some cases, special arrangements with the school need to be made, such as allowing the child untimed tests or doing alternate projects (see Shafron, 1998). Teachers might also be involved in the child's behavioral program.

Drug Treatment

Psychiatry's recent attention to drug treatment of OCD is unique in that much of the relevant work was carried out in pediatric populations (Rapoport, 1998). This review will mention established adult treatments, focusing on substantiation and application in children.

An initial trial of a serotonin reuptake inhibitor (SRI), most often a selective serotonin reuptake inhibitor (SSRI), is the treatment of choice. If there is no or only partial response to a SSRI at 10–12 weeks, another SSRI may be tried. In adults, augmentation with other agents is effective in partial responders, and some reports suggest augmentors are also useful for children.

SRIs. Clomipramine was the first SRI antidepressant to be shown effective for OCD, with subsequent controlled trials documenting anti-OCD effects of the SSRIs—(in order of increasing selectivity) fluoxetine, fluvoxamine, sertraline, and paroxetine. All have been studied in multi-center double-blind trials in adults (see Pigott & Seay, 1999). Citalopram, another SSRI, has been found effective for adults (see Montgomery, 1998). Controlled trials with children have been carried out for clomipramine, fluoxetine, fluvoxamine, and sertraline (see Table 2). Although the comparable study of paroxetine in children is still in progress, uncontrolled reports are also positive (Emslie et al., 1999). See D. A. Geller et al. (1998) and Thomsen (1998) for overviews.

Table 2 gives the dose range for adults, the most systematically obtained dosage data for children, and the recommended duration for a treatment trial. Low initial dosages, with slow upward titration, are the rule. Patients should be told initially that they may require a trial of more than one agent to find the best treatment for them, and the possibility of augmenting agents also should be suggested early. Not only may it be necessary to switch from one serotonin inhibitor to another, but combinations of the SRIs may help counterbalance differing adverse effects, although no systematic studies are available to document this widely held clinical belief (see below).

Trichotillomania. The first systematic drug treatment trial for trichotillomania found clomipramine superior to the selective norepinephrine reuptake inhibitor, desipramine, for 13 female patients (Swedo, Leonard, et al., 1989). Although individual case reports continued to support the finding that SRIs are beneficial (DeVane & Sallee, 1996; Gupta & Gupta, 1993), one 31-week, double-blind, placebo-controlled crossover study of fluoxetine using doses of up to 80 mg/day (23 adult patients, 16 of whom completed the trial) did not find fluoxetine effective (Streichenwein & Thornby, 1995).

Augmenting Strategies for Partial Responders

Because up to 50% of pediatric (and adult) cases show no or only partial response to initial SRI treatment (D. A. Geller et al., 1998), a variety of treatment modifications and augmentation strategies have evolved (see Rasmussen & Eisen, 1997, for an overview). At least two different SSRIs should be tried; if neither alone is sufficiently helpful, pharmacological augmentation is then appropriate.

Augmentation of SRIs with other agents. Augmentation of an SRI may be tried for patients with a partial response or intolerance to higher doses (see Table 2). In adults, two agents, clonazepam (Pigott, L'Heureux, Rubenstein, Hill, & Murphy, 1992) and haloperidol (McDougle et al., 1994) have been shown effective in controlled augmentation trials. See McDougle (1997) for a review of (predominantly adult) studies.

Clonazepam is a benzodiazepine with anxiolytic properties and serotonergic effects (Park et al., 1997; see March & Leonard, 1998). SRI augmentation in childhood-onset OCD has been described for a patient with onset of OCD symptoms at age 7 years but, other than psychotherapy, had no treatment for OCD until age 14 (Leonard et al., 1994). A variety of drug treatments, including buspirone augmentation, had been tried. At age 20, clonazepam (at doses gradually increasing to 6 mg/day) was instituted as an augmentor to fluoxetine (60 mg/day). Dramatic reduction in symptom severity was reported within 1 month and was maintained by 4 mg/day, as evaluated 1 year later.

Haloperidol as an augmentor was found most effective for adult patients with tics or a family history of tics (McDougle et al., 1994). In fact, recent research suggests that the distinction between "tic-related OCD" and "non-tic-related OCD" may be a useful one. OCD in the context of a personal or family history of tics and non-tic-related OCD may differ in terms of clinical phenomenology, neurobiology, and responsiveness to treatment, with tic-related OCD cases having a less satisfactory response to treatment with a SSRI alone (see King et al., 1998, for an overview). No controlled data on neuroleptic augmentation are available in children, however; and use in children should be done with care (Mandoki, 1995).

Because of concern about tardive dyskinesia, atypical antipsychotics such as *risperidone* have been tried. Recent trials have shown positive effects from risperidone augmentation of adult refractory OCD patients (e.g. McDougle et al., 1995; Ravizza, Barzega, Bellino, Bogetto, & Maina, 1996).

The role of risperidone augmentation in pediatric OCD requires further study (see Mandoki, 1995). However, risperidone augmentation of SRI treatment was helpful for four 8–13-year-old OCD cases described by Fitzgerald, Stewart, Tawile, and Rosenberg (1999). Two of these had comorbid tics, and three had aggressive behavior or violent images. Risperidone also was used in an 11-week open trial (Lombroso et al., 1995) for treatment of TD/tics in seven children and adolescents, three of whom also had OCD. One of these three had a 100% decrease in her OCD symptom severity (as measured by her endpoint CY-BOCS score, compared to baseline); the other two had slight but not significant improvements. These three (ages: 12, 13, and 16) were given a SRI and risperidone (1.5–2.5 mg/day). The risperidone was added to their concurrent SRI at 0.5 mg orally at bedtime, with scheduled increases of 0.5 mg every 5 days as tolerated up to a maximum of 2.5 mg/day in divided doses. The maintenance dose was generally achieved by 3 weeks and given on a twice-daily schedule. Weight gain ranging from 8 to 14 pounds occurred in all patients. Both haloperidol (mentioned above) and risperidone cause drowsiness, but weight gain may be an added concern with risperidone.

Addition of a second SRI has been used as an augmenting strategy in adults (e.g. Ravizza et al., 1996) and, to a limited extent, in children. In an open treatment trial of six adolescents (Simeon, Thatte, & Wiggins, 1990), combined fluoxetine and CMI allowed lower doses of both medicines and produced fewer side effects. Figueroa, Rosenberg, Birmaher, and Keshavan (1998) described an open series of seven patients, ages 9–23, given clomipramine and either fluoxetine, sertraline, fluvoxamine, or paroxetine and followed through between 5 and 22 months. This combination therapy appeared more effective than monotherapy for all cases. Although the evidence is still anecdotal, current effective use of combination therapy justifies its increased study, and double-blind controlled studies are indicated.

Intravenous clomipramine. Recent research (e.g. Koran, Sallee, & Pallanti, 1997; Sallee, Koran, Pallanti, Carson, & Sethuraman, 1998), including one placebo-controlled study (Fallon et al., 1998), indicates that intravenous (IV) clomipramine in adults both speeds initial response and converts nonresponders. Oral maintenance is still required. In the Fallon et al. study, 54 patients with oral clomipramine-refractory OCD received 14 infusions of either placebo or clomipramine, starting at 25 mg and increasing to 250 mg/day. Ratings were double-blind after infusion 14 ($N = 54$), single-blind 1 week later ($N = 39$), and non-blind at 1 month follow-up ($N = 31$). Twenty-one per cent of IV versus 0% of placebo cases were responders after 14 infusions. One month post-infusion (treatment not controlled), 58% were responders. There were no serious adverse events. The hypothesized mechanism involves the greater bioavailability of the more serotonergic parent compound clomipramine versus the more noradrenergic metabolite desmethylclomipramine, as a result of bypassing first-pass hepatoenteric metabolism.

In children, there have been small IV clomipramine studies with adolescents with depression or depression and OCD. In Sallee, Pollock, Perel, Ryan, and Stiller (1989), three of the five cases (age range = 17–19) studied had OCD as well as major depressive disorder, and parenteral clomipramine infusions of up to 200 mg/dose (1 mg/min) were administered without major adverse incident. One patient terminated the infusion due to nausea and vomiting. Two others also had complained of nausea after an initial 75 mg test dose during the first 15 to 20 minutes of infusion, but not during the second infusion (on night 2) of 200 mg. Drowsiness and sedation up to 18 hours later also were reported. In addition to amelioration of depression, the three with concurrent OCD had an immediate decrease in obsessive-compulsive symptoms. Follow-up at 6 months showed continued amelioration of OCD symptoms with oral clomipramine (350 mg/day) and no depressive symptoms.

In Sallee, Vrindavanam, Deas-Nesmith, Carson, and Sethuraman (1997), 2 of 16 adolescents had OCD among their comorbidities; one of these was in the single-dose 200 mg IV clomipramine treatment group. This case showed a decrease in depression and had a 50% decrease in Y-BOCS score by the sixth day. These reports justify

systematic studies for severely impaired refractory adolescent cases.

Maintenance Treatment

OCD is often chronic and long-term maintenance is to be anticipated. For example, Bolton, Luckie, and Steinberg (1995) report on a 9- to 14-year follow-up of 14 out of 15 cases initially treated in adolescence; the main (but not the only) treatments were behavior and family therapy, and 43% still met diagnostic criteria for OCD at follow-up. Adults who continue medication maintain their level of improvement achieved in short-term trials; lower doses may suffice and improve compliance (Ravizza et al., 1998). For such patients, drug discontinuation leads to relapse in 80% of cases at 2-year follow-up (Dolberg, Iancu, & Zohar, 1996). Skoog and Skoog (1999) provide a 40-year follow-up of OCD cases; 83% of cases improved, although few (20%) were asymptomatic.

The episodic course of OCD complicates treatment evaluation, but in adults who respond positively, medication should be continued for 1–2 years (Pato, Zohar-Kadouch, Zohar, & Murphy, 1988). In children, the need for long-term maintenance was documented by an 8-month study of 26 children and adolescents with severe OCD who had received clomipramine for a mean of 17.1 months (Leonard et al., 1991); a 2-month double-blind desipramine substitution resulted in 89% of the substituted (versus 18% of the nonsubstituted) subjects relapsing during the substitution phase. Concomitant CBT may lead to medication discontinuation for some patients (Stanley & Turner, 1995; Wever & Rey, 1997).

When discontinuation is attempted, tapering should be gradual, usually over several weeks. Long-term (i.e. indefinite) drug maintenance is suggested after two to four relapses, although systematic data are needed to support this. Most patients relapse within 2 months (Leonard et al., 1991).

Adverse effects of drug treatment. The SSRIs are recommended over clomipramine because of the tricyclic's anticholinergic, cardiovascular, sexual, and sedative effects. Clomipramine may be helpful when a tricyclic antidepressant (TCA) may benefit other psychiatric comorbidities and is less likely than SSRIs to cause insomnia, akathisia, nausea, or diarrhea (March & Leonard, 1998; also see Riddle, 1998; Thomsen, 1998). Because clomipramine has the potential for TCA-related cardiotoxic effects, pretreatment and periodic ECG and drug monitoring are necessary (B. Geller, Reising, Leonard, Riddle, & Walsh, 1999). Clomipramine's smaller margin of safety in cases of overdose is another concern.

The *side effect profiles of SSRIs*, in general, include drowsiness or insomnia, nausea, weight gain, agitation, and a host of less common events that should be reviewed with the patient and family. Although most adverse events occur within the first months of treatment, any can occur later. It is important for the family to be aware of this such that drug discontinuation is considered at all times during treatment.

There have been excellent reviews on the safety of the SRIs: clomipramine—DeVeaugh-Geiss et al., 1992; B. Geller et al., 1999; fluoxetine—D. A. Geller, Biederman, Reed, Spencer, and Wilens, 1995; Riddle et al., 1992; fluvoxamine—Goodman, Ward, Kablinger, and Murphy, 1997; Riddle et al., 1996; sertraline—Alderman, Wolkow, Chung, and Johnston, 1996, 1998; March et al., 1998; paroxetine—Gunasekara, Noble, and Benfield, 1998.

Augmenting agents. There is concern over dependency on clonazepam, although at the low doses used (see Table 2), this appears to be rare. Although haloperidol raises the concern of risk for tardive dyskinesia, the very low dose (often as low as 0.5 mg/day) and yearly 6-week drug holidays reduce this risk. Atypical agents such as risperidone may not be quite as effective augmenting agents for OCD and have their own risks of drowsiness and weight gain (Lombroso et al., 1995). In pediatric cases, risperidone may be more likely to cause dystonic reactions (Lombroso et al., 1995).

Drug interactions, toxicities, and adverse events. Drug interactions must be taken into account with regard to OCD treatment (e.g. Goodman et al., 1997). Although the SSRIs are similar pharmacodynamically, their pharmacokinetic profiles differ, with substantial differences in their potential for drug interactions via the inhibition of cytochrome P450 (CYP) isoenzymes (Lane, 1996). For example, fluoxetine and paroxetine are potent CYP2D6 inhibitors that may increase concentrations of other medications such as haloperidol, resperidone, or clomipramine. Fluvoxamine, a CYP3A4, CYP1A2, and CYP2C19 inhibitor, gives perhaps the greatest concern for drug interactions; it may, for example, increase blood concentration of theophylline.

Other pharmacokinetic features must be taken into account. For example, the elimination half-life of fluoxetine (in adults) is 1 to 3 days, but that of its active metabolite, norfluoxetine, is 7 to 15 days, making fluoxetine a desirable choice for patients who skip doses but problematic for those who may need to discontinue medication abruptly (Carpenter, McDougle, Epperson, & Price, 1996).

Drug Treatment and Comorbidities

Mania. SSRIs can trigger manic symptoms in adults (Berk, Koopowitz, & Szabo, 1996) and children (Diller & Avci, 1999; Go, Malley, Birmaher, & Rosenberg, 1998) treated for OCD with antidepressants. Alternately, a subgroup of OCD cases may be "prebipolar", independent of drug treatment. Additional investigation is needed to understand when such cases reflect drug effects or the unmasking of underlying bipolar mood disorder (see Berk et al., 1996).

ADHD. The high rate of comorbid ADHD means that stimulant drug treatment may be ongoing during OCD treatment. There is some evidence that stimulants may have an adverse effect on OCD (Joffe, Swinson, & Levitt, 1991), even triggering some compulsive or ritualistic behaviors (Borcherding et al., 1990).

Psychosis. Patients with schizophrenia being treated with clozapine (Baker et al., 1992) or risperidone (see Saxena, Wang, Bystritsky, & Baxter, 1996, and SRI augmentation section above) may have exacerbation of OCD; addition of typical neuroleptics may help this complication (Baker et al., 1992; Patel & Tandon, 1993).

Tic disorders. These will often necessitate trials of dopamine blocking agents. However, these may worsen anxiety symptoms (Blin, 1999) and necessitate discontinuation. The data on clonidine, which would be a logical alternative, are mixed (Hewlett, Vinogradov, & Agras, 1992; Hollander et al., 1991).

Substance abuse. OCD may be worsened or alleviated

Table 3
Criteria for Diagnosis of PANDAS[a]

- Prepubertal onset
- Presence of OCD and/or tics (lifetime diagnostic criteria met)
- Episodic clinical course (sudden and "explosive")
- At least two exacerbations occurring shortly after laboratory confirmation of group A beta-hemolytic streptococcal infection

Common but not required:

- When symptomatic, adventitious movements (motor hyperactivity and/or choreiform movements) may be present
- Attentional difficulties and emotional lability which fluctuate with exacerbations

[a] Based on Garvey et al., 1998.

by drugs of abuse and alcohol (Bollo, Cadet, & London, 1998; Burke, Burke, & Rae, 1994; Crum & Anthony, 1993; Delgado & Moreno, 1998; Fals-Stewart & Angarano, 1994). Where suspected or when the patient is nonresponsive, substance abuse should be considered and may need to be the prime target of treatment.

PANDAS

Patients with PANDAS present with OCD and/or a tic disorder typically of sudden onset and/or dramatic exacerbations in response to infection with group A beta-hemolytic streptococci (Swedo et al., 1998). Diagnostic criteria are shown in Table 3. Post-streptococcal autoimmunity has been proposed as one possible environmental trigger, and SC, the neurologic variant of rheumatic fever, has been the model for the pathophysiology of PANDAS (Swedo, 1994). In SC, molecular mimicry is thought to play a role through a process in which antibodies raised against the group A beta-hemolytic streptococci cross-react with neuronal cells and produce inflammation in the central nervous system, particularly within the basal ganglia (Husby, van de Rijn, Zabriskie, Abdin, & Williams, 1976). As 70% of SC patients have OCD (Swedo, 1994), and as post-streptococcal exacerbation is seen in OCD/tic patients without a history of SC, the notion that some OCD and tic cases are variants of SC has also been proposed.

The proposed autoimmune model is of clinical interest as it leads to the hypothesis that, as for SC and other autoimmune diseases, immunosuppressant treatment would be helpful. Recently, intravenous immunoglobulin (IVIG) and plasma exchange (PEX) have been shown to be effective (Perlmutter et al., in press). A total of 30 children (age 5–14) with streptococcal-related OCD/tics, all with pre-pubertal onset, received IVIG ($N = 9$ [9 of 10 randomized to IVIG completed the trial]), PEX ($N = 10$), or placebo IVIG ($N = 10$). At both 1 month and 12 months after therapy, the results indicated striking and sustained improvement on active treatment, virtually without placebo effect. In some cases, these improvements were paralleled by reduction in basal ganglia volume (Giedd, Rapoport, Leonard, Richter, & Swedo, 1996). Although these results are exciting, it is not yet clear how large a fraction of childhood OCD cases are PANDAS.

A related study is an ongoing trial of penicillin prophylaxis for PANDAS, which may help children with regular infection-related worsening of their OCD. A pilot study with (250 mg, twice daily) oral penicillin V (Garvey et al., 1999) was insufficient to achieve an adequate level of streptococcal prophylaxis and was therefore inconclusive. A new study with higher doses, other antibiotics, and a large sample is ongoing.

Investigative Treatments

New agents. Tramadol: recent research suggests that OCD may be, in part, mediated by the opioid system (Insel & Pickar, 1983; Shapira et al., 1997). Because the opioid antagonist naloxone exacerbates OCD in some patients, an open trial of the opioid agonist tramadol was carried out for seven treatment-refractory adult OCD patients (with a variety of comorbidities including tics or TD) (Shapira et al., 1997). (Tramadol has been used primarily for analgesia, but it also inhibits the reuptake of norepinephrine and serotonin.) Six of Shapira et al.'s seven cases completed at least 2 weeks of treatment, with mean dose of 250 mg/day tramadol (in three to four divided doses). These six reported a diminuation in obsessions and in the urge to perform their compulsions. One (who had a history of panic attacks) discontinued medication during week 6 after experiencing an attack. The dose-limiting side effect was sedation, but the drug was generally well tolerated. If, as suggested, the mechanism of action is distinct from the SRIs, tramadol may prove valuable. There are no pediatric data for tramadol and OCD.

Transcranial magnetic stimulation (TMS). TMS, involving noninvasive and focal stimulation of the brain, uses powerful magnetic fields to alter brain activity. It is a promising research tool and therapeutic agent for a variety of disorders involving mood and anxiety (George, Lisanby, & Sackeim, 1999). In adult OCD patients (Cora-Locatelli et al., 1998; Greenberg et al., 1997), a single session of right prefrontal rTMS (repetitive TMS) decreased compulsive urges for 8 hours (Greenberg & Rauch, in press). TMS has not yet been examined for treatment-refractory cases, and there are no data for children.

Neurosurgery. In adults, neurosurgery is still employed for treatment-refractory OCD (see Jenike, 1998, for a review), with capsulotomy the most common procedure (Mindus, Edman, & Andreewitch, 1999). Dramatic technological improvements in this arena include stereotactic MRI localization of the lesions, and radiosurgery ("gamma knife") eliminates the need for craniotomy as the lesions are produced by cross-firing of cobalt-60 gramma irradiation. The effectiveness of these surgeries can ultimately only be judged double-blind. To date, no such studies have been completed and, until this is the case, this treatment must be considered experimental. These procedures, which involve irreversible techniques, have not and are unlikely to be studied in children; the effect on the developing central nervous system is unknown.

Concluding Comments

In the past decade, greater attention has been given to childhood OCD than to any other childhood anxiety disorder. This is due to the awareness of the frequency of the disorder and the approval of several new drugs for pediatric OCD.

Behavioral treatment of children and adolescents is the preference of most patients and practitioners. However, none of the behavioral studies to date meet the criteria for rigorous research used in adults, and most are clinical reports or adaptations of techniques. These are nonetheless clinically compelling, and a systematic study is now in progress. This new pediatric trial of behavioral treatment will provide welcome guidelines that will also refine treatment assignment in this domain.

Drug treatment studies are easier to conduct and easier to translate into clinical practice. The indisputable efficacy for SRIs has produced perhaps an overenthusiasm for drug treatment. In the U.S., polypharmacy is becoming more common in child psychiatry, partially as a result of treating comorbid disorders. There are only limited data about the efficacy and safety of these combinations, and prescribing combined psychotropic medications to children should be done only by physicians who are trained in pharmacotherapy and familiar with known drug interactions and the limited data available (Wilens, Spencer, Biederman, Wozniak, & Connor, 1995). Nevertheless, severe cases will benefit from the advances in drug treatment, particularly the uses of augmenting agents.

Novel research on a possible autoimmune subgroup of OCD is intriguing and brings new treatments. Here, too, the treatments need replication, and most children with OCD are unlikely to be in this autoimmune subgroup.

Future treatments of OCD, whether in adults or children, will most likely follow further subtyping with increasing sophistication as to which types of OCD respond best to which treatment. We already have learned that age of onset (pre- vs. post-pubertal) and pattern of comorbidities (e.g. OCD/TD or tics) provide guidance as to treatment. At the same time, increasingly sophisticated brain imaging techniques are further refining the circuits of pediatric OCD (see Rosenberg & Keshavan, 1998) and will hopefully inform treatment development.

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